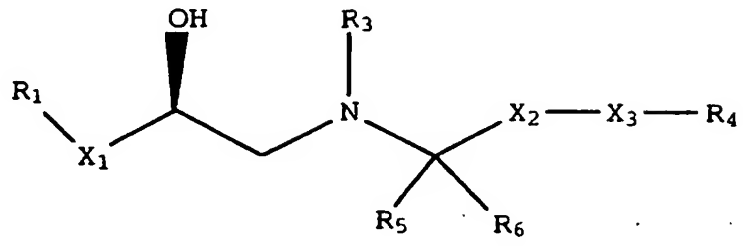
We claim:

1. A method of stimulating the β_3 receptor which comprises administering to a patient in need thereof a compound of Formula I:



(I)

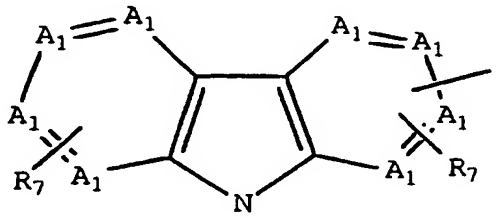
wherein:

X_1 is $-OCH_2-$, $-SCH_2-$, or a bond;

X_2 is a bond, or a 1 to 5 carbon straight or branched alkylene;

X_3 is O, S, or a bond;

R_1 is a fused heterocycle of the formula:

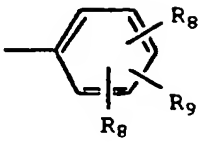
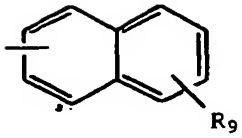
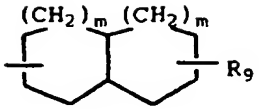
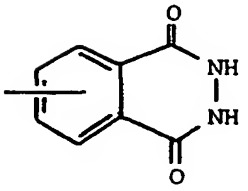
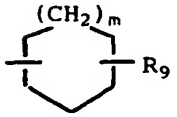
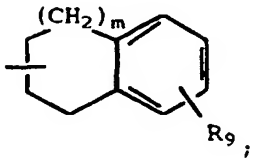


the A_1 groups are independently carbon or nitrogen, provided that no more than 2 nitrogens may be contained in either fused 6 membered ring and those 2 nitrogens may not be adjacent;

R_2 is independently hydrogen, C_1-C_4 alkyl, or aryl;

R_3 is hydrogen or C_1-C_4 alkyl;

R_4 is an optionally substituted heterocycle or a moiety selected from the group consisting of:

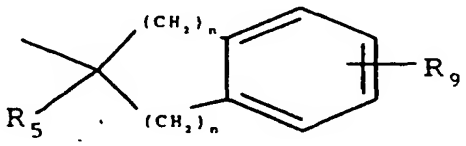
R_5 is hydrogen or C_1-C_4 alkyl;

R_6 is hydrogen, C_1-C_4 alkyl, or CO_2(C_1-C_4 alkyl);

or R_5 and R_6 combine with the carbon to which each is attached to form a C_3-C_6 cycloalkyl;

or R_6 combines with X_2 and the carbon to which each is attached to form a C_3-C_8 cycloalkyl;

or R_6 combines with X_2, R_4, and the carbon to which each is attached to form:



provided that R_5 is hydrogen;

R_7 is independently hydrogen, halo, hydroxy, OR_2, C_1-C_4 alkyl, C_1-C_4 haloalkyl, aryl, $COOR_2$, $CONR_2R_2$, $NHCOR_2$, C_1-C_4 alkoxy, NHR_2, SR_2, CN, SO_2R_2, SO_2NHR_2, or SOR_2;

R_8 is independently hydrogen, halo, or C_1-C_4 alkyl;

R_9 is hydrogen, halo, hydroxy, CN, OR_{10}, C_1-C_4 alkyl, C_1-C_4 haloalkyl, CO_2R_2, $CONR_{11}R_{12}$, CONH(C_1-C_4 alkyl or C_1-C_4 alkoxy), SR_2, $CSNR_2$, $CSNR_{11}R_{12}$, $NR_2SO_2R_2$, SO_2R_2, $SO_2NR_{11}R_{12}$, SOR_2, $NR_{11}R_{12}$, optionally substituted aryl, optionally substituted heterocycle, or C_2-C_4 alkenyl substituted with CN, CO_2R_2 or $CONR_{11}R_{12}$;

R_{10} is C_1-C_4 alkyl, C_1-C_4 haloalkyl, $(CH_2)_nC_3$-C_8 cycloalkyl, $(CH_2)_n$aryl, $(CH_2)_n$heterocycle, $(CH_2)_nC_3$-C_8 optionally substituted cycloalkyl, $(CH_2)_n$ optionally substituted aryl, $(CH_2)_n$ optionally substituted heterocycle, or $(CH_2)_nCO_2R_2$;

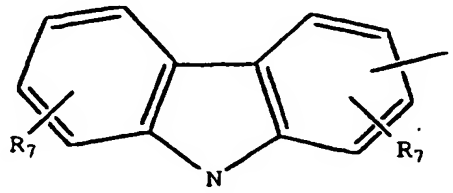
R_{11} and R_{12} are independently hydrogen, C_1-C_4 alkyl, aryl, $(CH_2)_n$aryl, or combine with the nitrogen to which each is bound to form morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl;

m is 0 or 1;

n is independently 0, 1, 2, or 3;

or a pharmaceutically acceptable salt or solvate thereof.

2. The method of Claim 1 wherein R_1 is

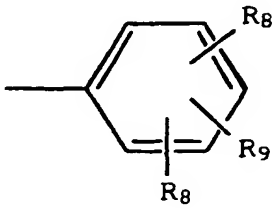


3. The method of Claim 2 wherein R_7 is hydrogen and R_3 is hydrogen.

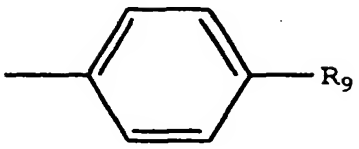
4. The method of Claim 3 wherein X_3 is O or a bond.

5. The method of Claim 4 wherein R_5 and R_6 are methyl, X_2 is methylene or ethylene, and X_3 is a bond.

6. The method of Claim 5 wherein R_4 is



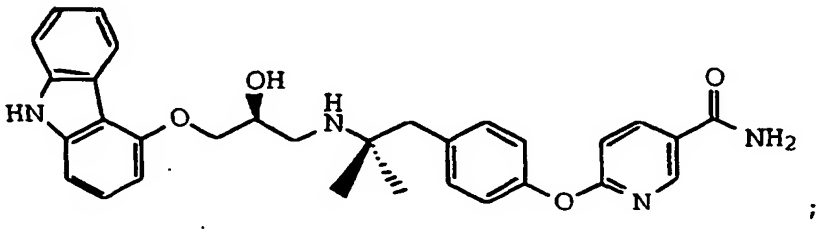
7. The method of Claim 6 wherein R_4 is



and R_9 is OR_{10} or $NR_2SO_2R_2$.

8. The method of Claim 7 wherein R_{10} is phenyl or pyridyl said phenyl or pyridyl being substituted with CN, hydroxy, $CONR_{11}R_{12}$, CO_2R_2, SO_2R_2, or $SO_2NR_{11}R_{12}$.

9. The method of Claim 8 wherein the compound is:



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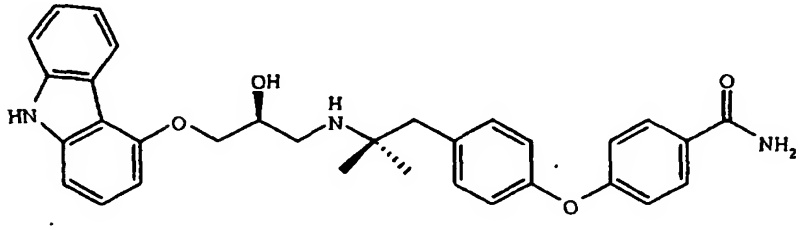
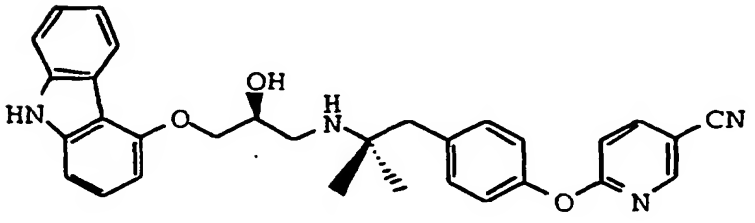
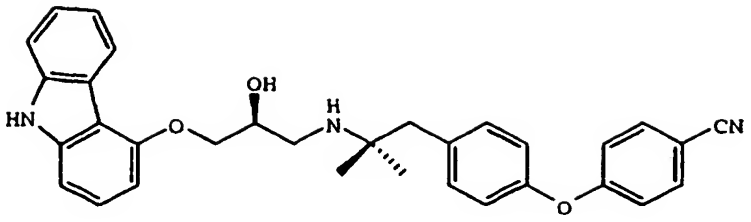


;

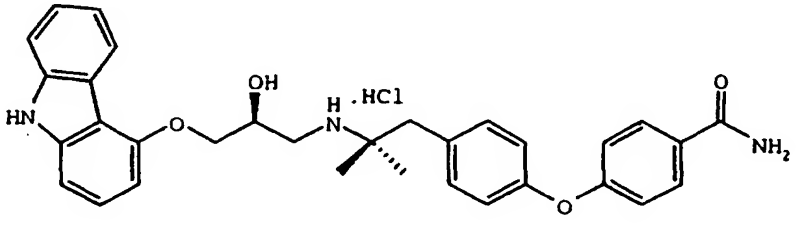


;

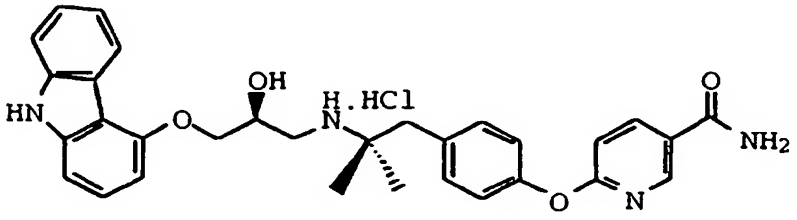


;

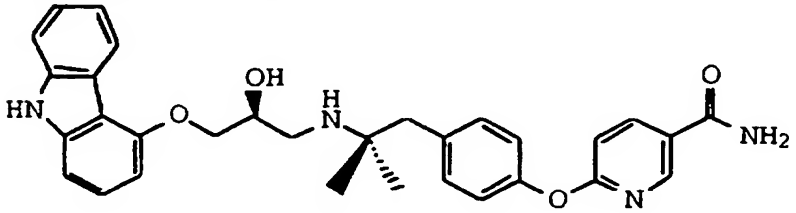
or a pharmaceutically acceptable salt or solvate thereof; or



; or

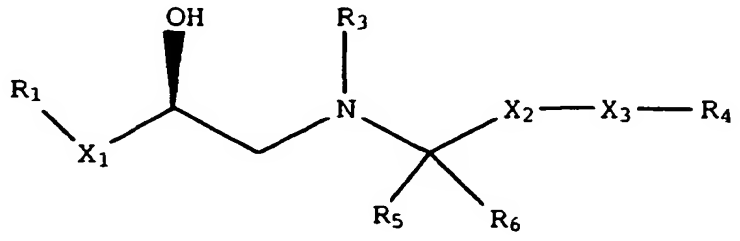


10. The method of claim 9 wherein the compound is



or a pharmaceutically acceptable salt or solvate.

11. A method of treating obesity which comprises administering to a patient in need thereof a compound of Formula I:



(I)

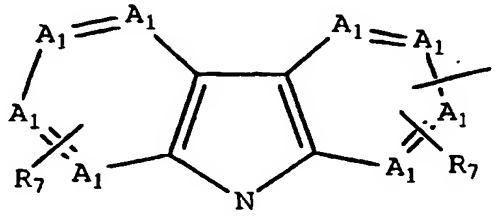
wherein:

X_1 is $-OCH_2-$, $-SCH_2-$, or a bond;

X_2 is a bond, or a 1 to 5 carbon straight or branched alkylene;

X_3 is O, S, or a bond;

R_1 is a fused heterocycle of the formula:

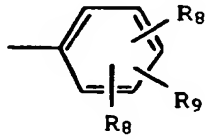


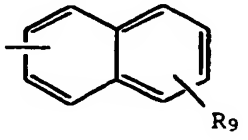
the A_1 groups are independently carbon or nitrogen, provided that no more than 2 nitrogens may be contained in either fused 6 membered ring and those 2 nitrogens may not be adjacent;

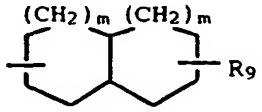
R_2 is independently hydrogen, C_1-C_4 alkyl, or aryl;

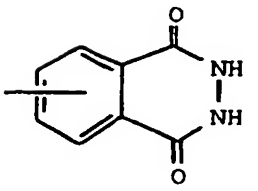
R_3 is hydrogen or C_1-C_4 alkyl;

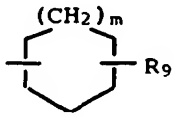
R_4 is an optionally substituted heterocycle or a moiety selected from the group consisting of:

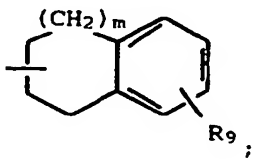












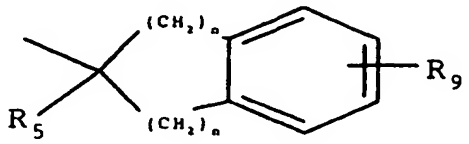
R_5 is hydrogen or C_1-C_4 alkyl;

R_6 is hydrogen, C_1-C_4 alkyl, or $CO_2(C_1$-C_4 alkyl);

or R_5 and R_6 combine with the carbon to which each is attached to form a C_3-C_6 cycloalkyl;

or R_6 combines with X_2 and the carbon to which each is attached to form a C_3-C_8 cycloalkyl;

or R_6 combines with X_2, R_4, and the carbon to which each is attached to form:



provided that R_5 is hydrogen;

R_7 is independently hydrogen, halo, hydroxy, OR_2, C_1-C_4 alkyl, C_1-C_4 haloalkyl, aryl, $COOR_2$, $CONR_2R_2$, $NHCOR_2$, C_1-C_4 alkoxy, NHR_2, SR_2, CN, SO_2R_2, SO_2NHR_2, or SOR_2;

R_8 is independently hydrogen, halo, or C_1-C_4 alkyl;

R_9 is hydrogen, halo, hydroxy, CN, OR_{10}, C_1-C_4 alkyl, C_1-C_4 haloalkyl, CO_2R_2, $CONR_{11}R_{12}$, $CONH(C_1$-C_4 alkyl or C_1-C_4 alkoxy), SR_2, $CSNR_2$, $CSNR_{11}R_{12}$, $NR_2SO_2R_2$, SO_2R_2, $SO_2NR_{11}R_{12}$, SOR_2, $NR_{11}R_{12}$, optionally substituted aryl, optionally substituted heterocycle, or C_2-C_4 alkenyl substituted with CN, CO_2R_2 or $CONR_{11}R_{12}$;

R_{10} is C_1-C_4 alkyl, C_1-C_4 haloalkyl, $(CH_2)_nC_3$-C_8 cycloalkyl, $(CH_2)_n$aryl, $(CH_2)_n$heterocycle, $(CH_2)_nC_3$-C_8 optionally substituted cycloalkyl, $(CH_2)_n$ optionally substituted aryl, $(CH_2)_n$ optionally substituted heterocycle, or $(CH_2)_nCO_2R_2$;

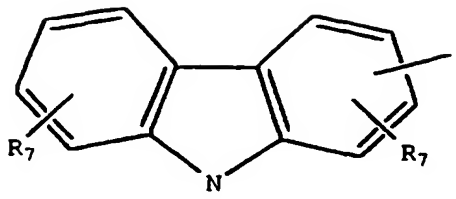
R_{11} and R_{12} are independently hydrogen, C_1-C_4 alkyl, aryl, $(CH_2)_n$aryl, or combine with the nitrogen to which each is bound to form morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl;

m is 0 or 1;

n is independently 0, 1, 2, or 3;

or a pharmaceutically acceptable salt or solvate thereof.

12. The method of Claim 11 wherein R_1 is

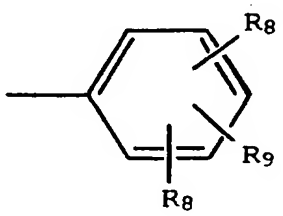


13. The method of Claim 12 wherein R_7 is hydrogen and R_3 is hydrogen.

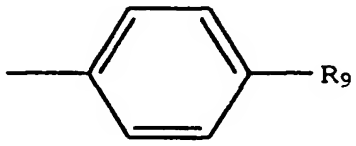
14. The method of Claim 13 wherein X_3 is O or a bond.

15. The method of Claim 14 wherein R_5 and R_6 are methyl, X_2 is methylene or ethylene, and X_3 is a bond.

16. The method of Claim 15 wherein R_4 is



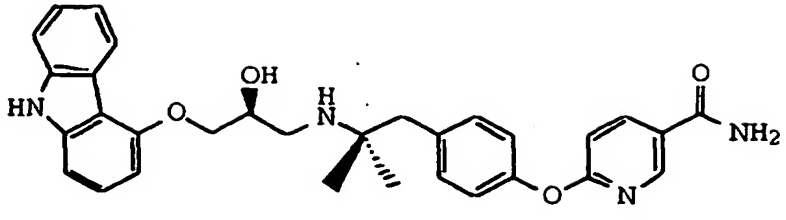
17. The method of Claim 16 wherein R_4 is



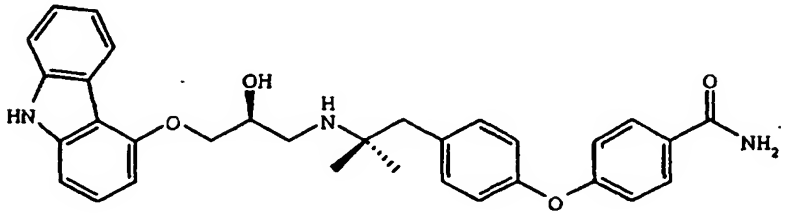
and R_9 is OR_{10} or $NR_2SO_2R_2$.

18. The method of Claim 17 wherein R_{10} is phenyl or pyridyl said phenyl or pyridyl being substituted with CN, hydroxy, $CONR_{11}R_{12}$, CO_2R_2, SO_2R_2, or $SO_2NR_{11}R_{12}$.

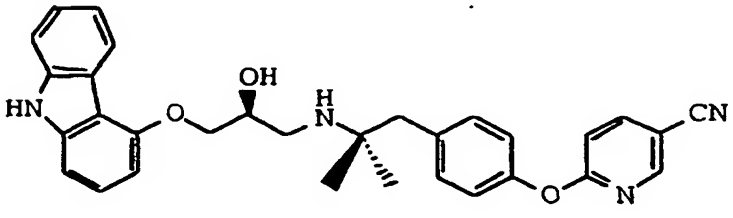
19. The method of Claim 18 wherein the compound is:



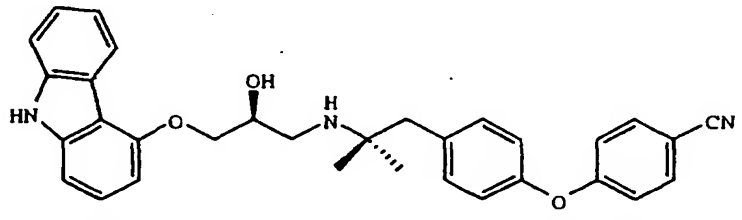
;



;

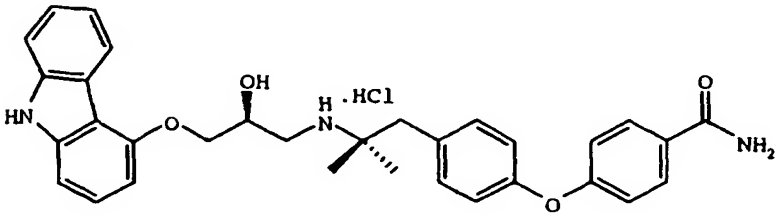


;

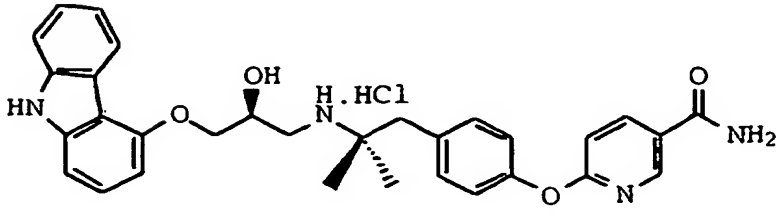


;

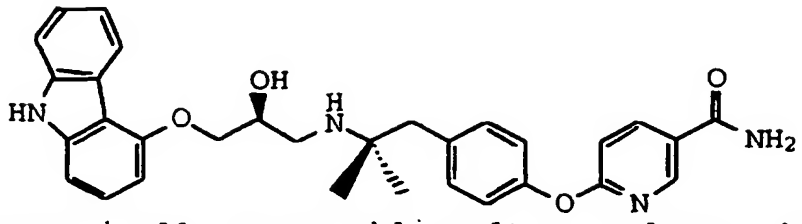
or a pharmaceutically acceptable salt or solvate thereof; or



; or

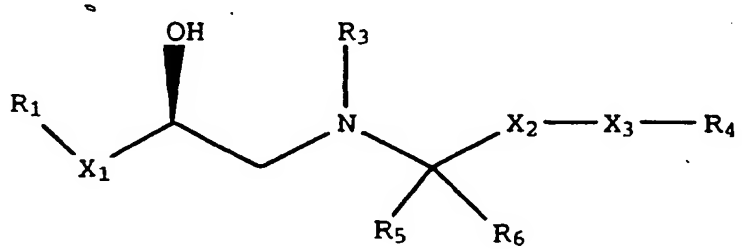


20. The method of claim 19 wherein the compound is



or a pharmaceutically acceptable salt or solvate thereof.

21. A method of treating Type II diabetes which comprises administering to a patient in need thereof a compound of Formula I:



(I)

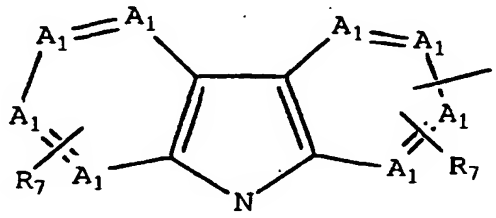
wherein:

X_1 is $-OCH_2-$, $-SCH_2-$, or a bond;

X_2 is a bond, or a 1 to 5 carbon straight or branched alkylene;

X_3 is O, S, or a bond;

R_1 is a fused heterocycle of the formula:

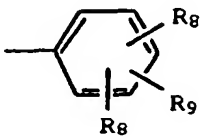
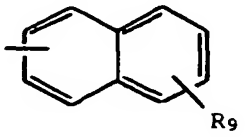
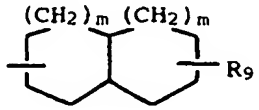
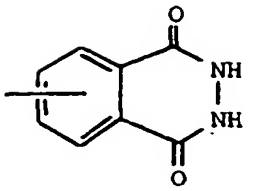
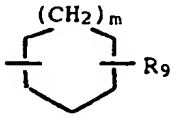
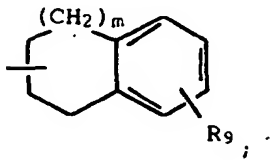


the A_1 groups are independently carbon or nitrogen, provided that no more than 2 nitrogens may be contained in either fused 6 membered ring and those 2 nitrogens may not be adjacent;

R_2 is independently hydrogen, C_1-C_4 alkyl, or aryl;

R_3 is hydrogen or C_1-C_4 alkyl;

R_4 is an optionally substituted heterocycle or a moiety selected from the group consisting of:

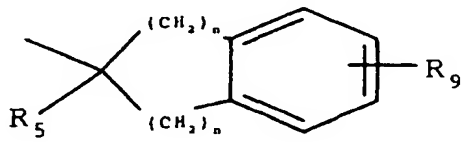
R_5 is hydrogen or C_1-C_4 alkyl;

R_6 is hydrogen, C_1-C_4 alkyl, or CO_2(C_1-C_4 alkyl);

or R_5 and R_6 combine with the carbon to which each is attached to form a C_3-C_6 cycloalkyl;

or R_6 combines with X_2 and the carbon to which each is attached to form a C_3-C_8 cycloalkyl;

or R_6 combines with X_2, R_4, and the carbon to which each is attached to form:



provided that R_5 is hydrogen;

R_7 is independently hydrogen, halo, hydroxy, OR_2, C_1-C_4 alkyl, C_1-C_4 haloalkyl, aryl, $COOR_2$, $CONR_2R_2$, $NHCOR_2$, C_1-C_4 alkoxy, NHR_2, SR_2, CN, SO_2R_2, SO_2NHR_2, or SOR_2;

R_8 is independently hydrogen, halo, or C_1-C_4 alkyl;

R_9 is hydrogen, halo, hydroxy, CN, OR_{10}, C_1-C_4 alkyl, C_1-C_4 haloalkyl, CO_2R_2, $CONR_{11}R_{12}$, CONH(C_1-C_4 alkyl or C_1-C_4 alkoxy), SR_2, $CSNR_2$, $CSNR_{11}R_{12}$, $NR_2SO_2R_2$, SO_2R_2, $SO_2NR_{11}R_{12}$, SOR_2, $NR_{11}R_{12}$, optionally substituted aryl,

optionally substituted heterocycle, or C_2-C_4 alkenyl substituted with CN, CO_2R_2 or $CONR_{11}R_{12}$;

R_{10} is C_1-C_4 alkyl, C_1-C_4 haloalkyl, $(CH_2)_nC_3$-C_8 cycloalkyl, $(CH_2)_n$aryl, $(CH_2)_n$heterocycle, $(CH_2)_nC_3$-C_8 optionally substituted cycloalkyl, $(CH_2)_n$ optionally substituted aryl, $(CH_2)_n$ optionally substituted heterocycle, or $(CH_2)_nCO_2R_2$;

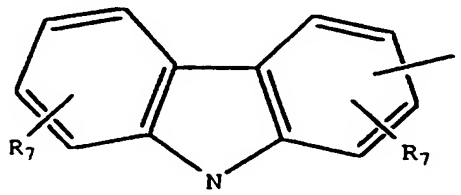
R_{11} and R_{12} are independently hydrogen, C_1-C_4 alkyl, aryl, $(CH_2)_n$aryl, or combine with the nitrogen to which each is bound to form morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl;

m is 0 or 1;

n is independently 0, 1, 2, or 3;

or a pharmaceutically acceptable salt or solvate thereof.

22. The method of Claim 21 wherein R_1 is

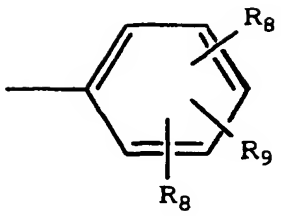


23. The method of Claim 22 wherein R_7 is hydrogen and R_3 is hydrogen.

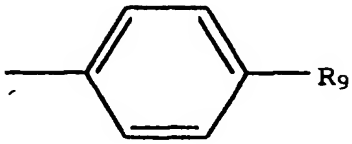
24. The method of Claim 23 wherein X_3 is O or a bond.

25. The method of Claim 24 wherein R_5 and R_6 are methyl, X_2 is methylene or ethylene, and X_3 is a bond.

26. The method of Claim 25 wherein R_4 is



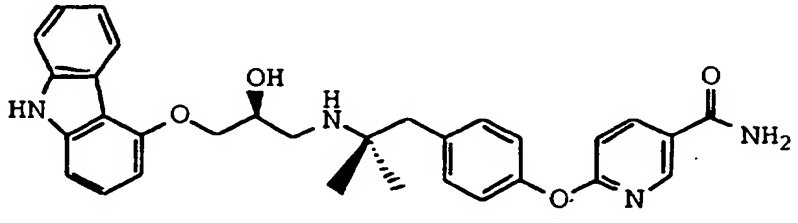
27. The method of Claim 26 wherein R_4 is



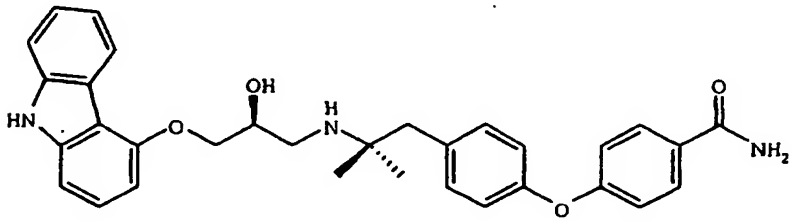
and R_9 is OR_{10} or $NR_2SO_2R_2$.

28. The method of Claim 27 wherein R_{10} is phenyl or pyridyl said phenyl or pyridyl being substituted with CN, hydroxy, $CONR_{11}R_{12}$, CO_2R_2, SO_2R_2, or $SO_2NR_{11}R_{12}$.

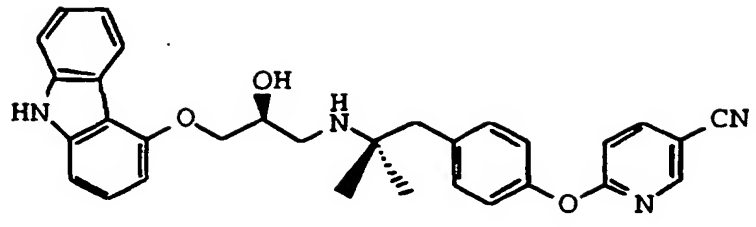
29. The method of Claim 28 wherein the compound is:



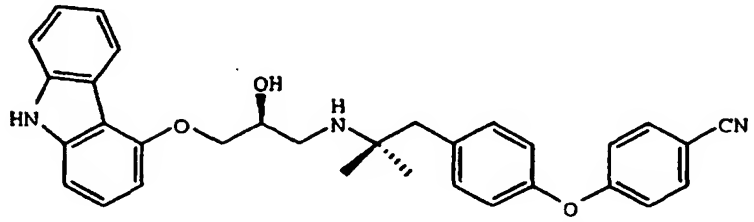
;



;

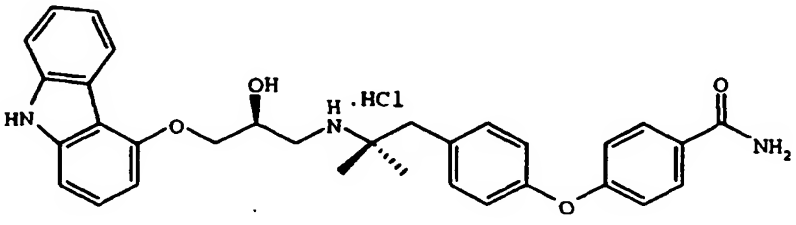


;

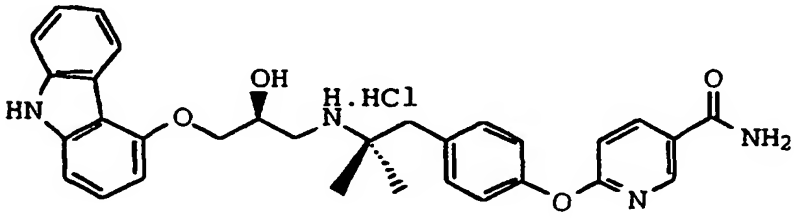


;

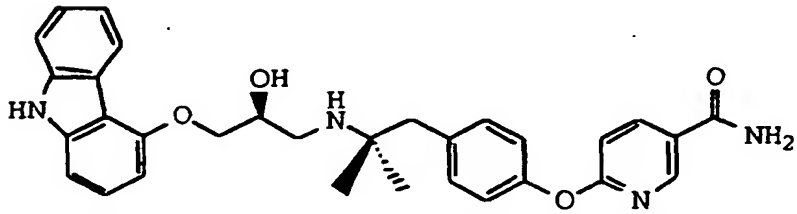
or a pharmaceutically acceptable salt or solvate thereof; or



; or

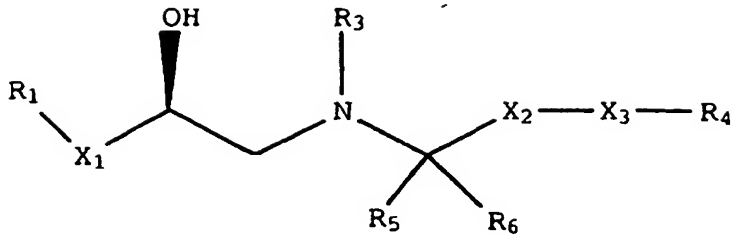


30. The method of claim 29 wherein the compound is



or a pharmaceutically acceptable salt or solvate.

31. A compound of the Formula II



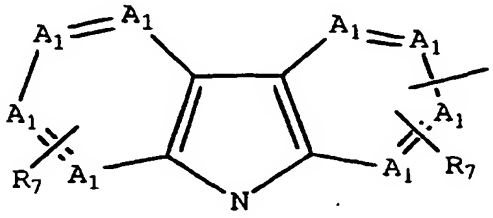
(II)

wherein:

X_1 is $-OCH_2-$, $-SCH_2-$, or a bond;

X_3 is O, S, or a bond;

R_1 is a fused heterocycle of the formula:

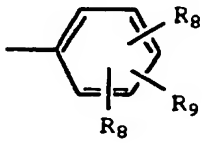


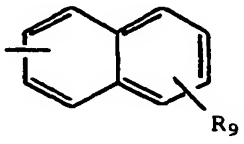
the A_1 groups of said heterocycle are independently carbon or nitrogen, provided that no more than 2 nitrogens may be contained in either fused 6 membered ring and those 2 nitrogens may not be adjacent;

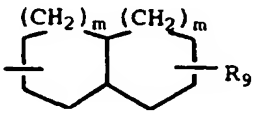
R_2 is independently hydrogen, C_1-C_4 alkyl, or aryl;

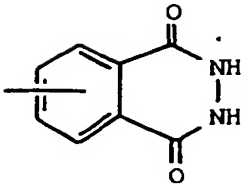
R_3 is hydrogen or C_1-C_4 alkyl;

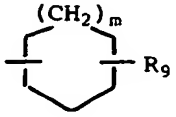
R_4 is an optionally substituted heterocycle or a moiety selected from the group consisting of:

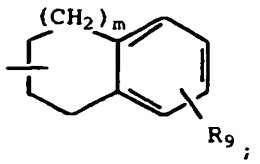












;

X_2 is a bond, or a 1 to 5 carbon straight or branched alkylene;

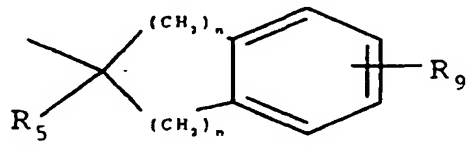
R_5 is hydrogen or C_1-C_4 alkyl;

R_6 is hydrogen, C_1-C_4 alkyl, or CO_2(C_1-C_4 alkyl);

or R_5 and R_6 combine with the carbon to which each is attached to form a C_3-C_6 cycloalkyl;

or R_6 combines with X_2 and the carbon to which each is attached to form a C_3-C_8 cycloalkyl;

or R_6 combines with X_2, R_4, and the carbon to which each is attached to form:



provided that R_5 is hydrogen;

R_7 is independently hydrogen, halo, hydroxy, OR_2, C_1-C_4 alkyl, C_1-C_4 haloalkyl, aryl, $COOR_2$, $CONHR_2$, $NHCOR_2$, C_1-C_4 alkoxy, NHR_2, SR_2, CN, SO_2R_2, SO_2NHR_2, or SOR_2;

R_8 is independently hydrogen, halo or C_1-C_4 alkyl;

R_9 is halo, CN, OR_{10}, C_1-C_4 alkyl, C_1-C_4 haloalkyl, CO_2R_2, $CONR_{11}R_{12}$, CONH(C_1-C_4 alkyl or C_1-C_4 alkoxy), SR_2, $CSNR_2$, $CSNR_{11}R_{12}$, $NR_2SO_2R_2$, SO_2R_2, $SO_2NR_{11}R_{12}$, SOR_2, $NR_{11}R_{12}$, optionally substituted aryl, optionally substituted heterocycle, or C_2-C_4 alkenyl substituted with CN, CO_2R_2 or $CONR_{11}R_{12}$;

R_{10} is C_1-C_4 alkyl, C_1-C_4 haloalkyl, $(CH_2)_nC_3$-C_8 cycloalkyl, $(CH_2)_n$aryl, $(CH_2)_n$heterocycle, $(CH_2)_nC_3$-C_8 optionally substituted cycloalkyl, $(CH_2)_n$ optionally substituted aryl, $(CH_2)_n$ optionally substituted heterocycle, or $(CH_2)_nCO_2R_2$;

R_{11} and R_{12} are independently hydrogen, C_1-C_4 alkyl, aryl, $(CH_2)_n$aryl, or combine with the nitrogen to which each is bound to form morpholinyl, piperidinyl, pyrrolidinyl, or piperazinyl;

m is 0 or 1;

n is independently 0, 1, 2, or 3;

provided:

when R_5 or R_6 is hydrogen; either

1) one or more A_1 must be nitrogen,

or

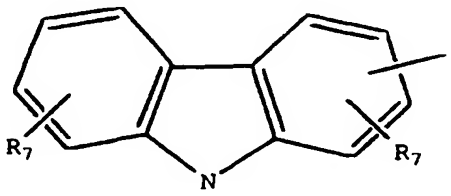
2) R_9 is CN, OR_{10}, CO_2R_2, $CSNR_2$, $CSNR_{11}R_{12}$, $NR_2SO_2R_2$, $SO_2NR_{11}R_{12}$, optionally substituted aryl, optionally substituted heterocycle, or C_2-C_4 alkenyl substituted with CN, CO_2R_2 or $CONR_{11}R_{12}$; and

R_{10} is C_1-C_4 haloalkyl, $(CH_2)_nC_3$-C_8 cycloalkyl, $(CH_2)_n$heterocycle, $(CH_2)_nC_3$-C_8 optionally substituted cycloalkyl, $(CH_2)_n$ optionally substituted aryl, or $(CH_2)_n$ optionally substituted heterocycle;

or a pharmaceutically acceptable salt or solvate thereof.

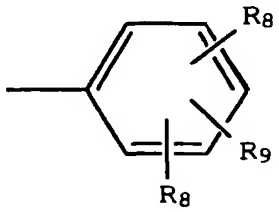
32. A compound of Claim 31 wherein R_5 and R_6 are methyl or ethyl.

33. A compound of Claim 32 wherein R_1 is

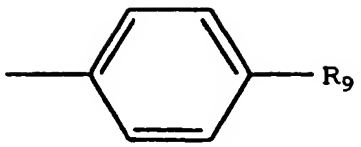


34. A compound of Claim 33 wherein X_2 is methylene or ethylene.

35. A compound of Claim 34 wherein R_4 is



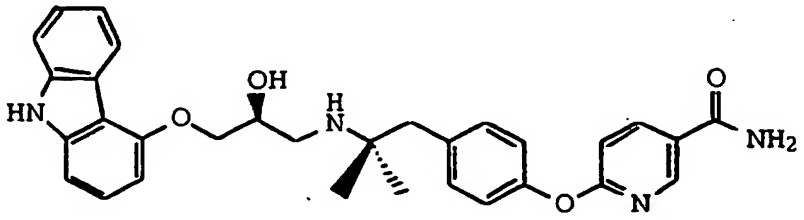
36. A compound of Claim 35 wherein R_4 is

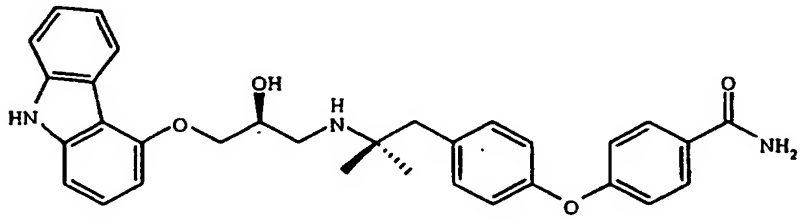


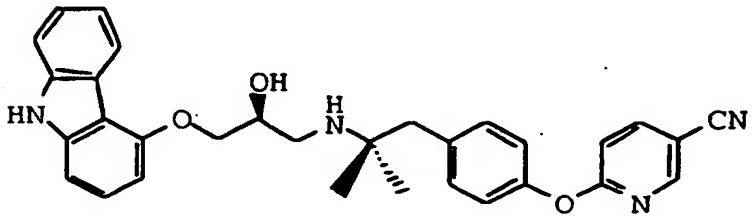
and R_9 is OR_{10} or $NR_2SO_2R_2$.

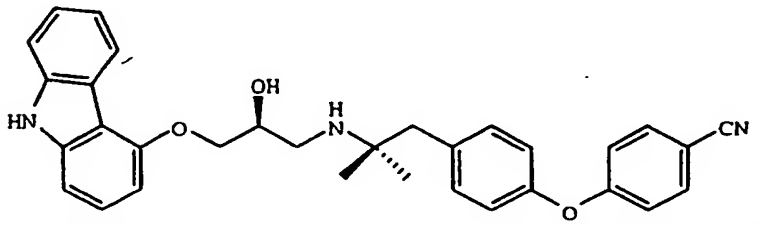
37. A compound of Claim 36 wherein R_{10} is phenyl or pyridyl said phenyl or pyridyl being substituted with CN, $CONR_{11}R_{12}$, CO_2R_2, SO_2R_2, or $SO_2NR_{11}R_{12}$.

38. A compound of Claim 37 which is:

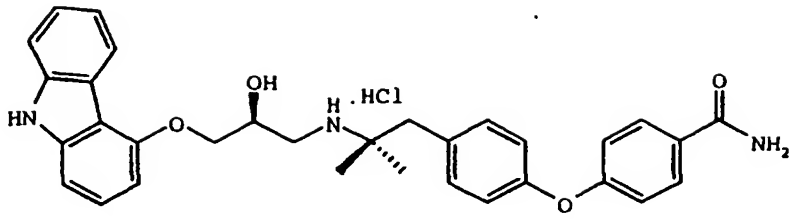

;


;

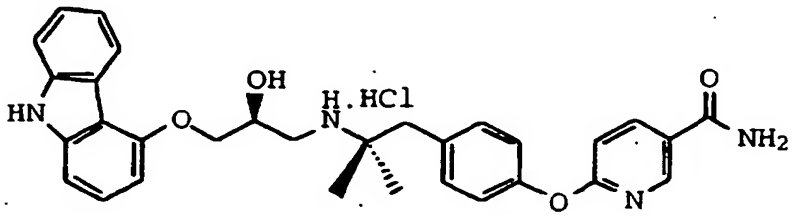

;


;

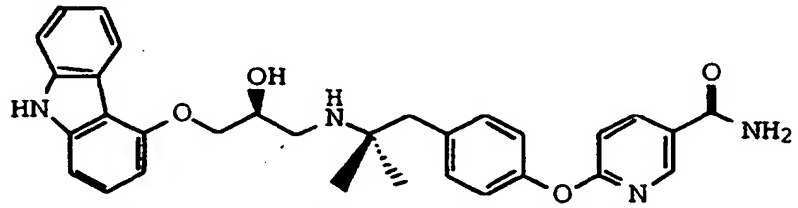
or a pharmaceutically acceptable salt or solvate thereof; or



; or



39. The compound of claim 38 of the formula



or a pharmaceutically acceptable salt or solvate.

40. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 31, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

41. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 32, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

42. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 33, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

43. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 34, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

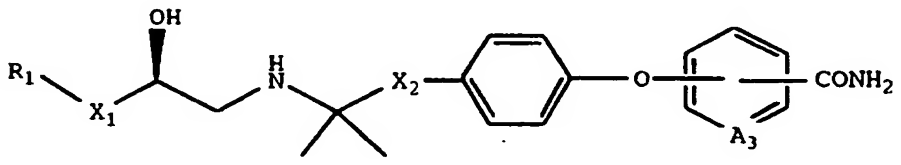
44. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 35, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

45. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 36, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

46. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 38, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

47. A pharmaceutical formulation comprising as an active ingredient a compound of Claim 39, associated with one or more pharmaceutically acceptable carriers, excipients or diluents.

48. A process of preparing a compound of claim 31 of the formula III:



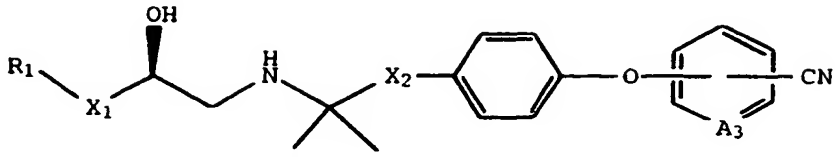
(III)

wherein:

A3 is CH or N;

which comprises:

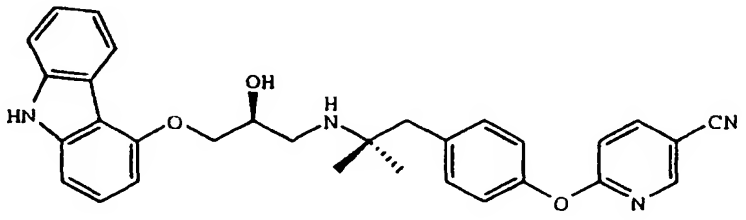
in step 1, hydrolysis of a compound of the formula:



;

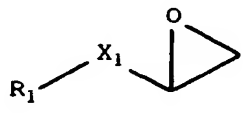
and optionally in step 2, reacting the product of step 1 with an acid to form an acid addition salt.

49. The process of claim 48 wherein in step 1 the hydrolysis is of a compound of the formula



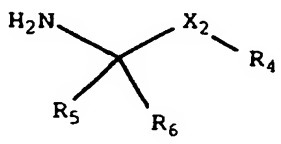
50. A process of preparing a compound of Claim 31, which comprises:

in step 1, reacting an epoxide of the formula XI:



(XI)

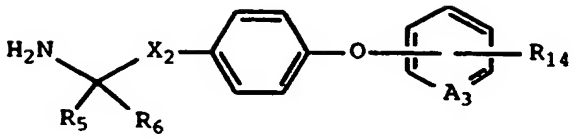
with an amine of formula B:



(B);

and optionally in step 2, reacting the product of step 1 with an acid to form an acid addition salt.

51. A process of Claim 50, wherein the amine is of the formula:



wherein:

A_3 is CH or N;

R_{14} is C_1-C_4 alkyl, C_1-C_4 haloalkyl, hydroxy, carboxy, tetrazolyl, acyl, $COOR_2$, $CONR_{11}R_{12}$, $CONH(C_1$-C_4 alkoxy), cyano, C_1-C_4 alkoxy, C_1-C_4 alkyl, phenyl, nitro, $NR_{11}R_{12}$, $NHCO(C_1$-C_4 alkyl), NHCO(benzyl), NHCO(phenyl), SR_2, $S(C_1$-C_4 alkyl), $OCO(C_1$-C_4 alkyl), $SO_2(NR_{11}R_{12})$, $SO_2(C_1$-C_4 alkyl), or SO_2(phenyl).

52. The process of claim 50 wherein;

A_3 is N; and

R_{14} is $COOR_2$, $CONR_{11}R_{12}$, $CONH(C_1$-C_4 alkoxy), or cyano.